

Remarks

After amendment, claims 6-9, 25 and 27-30 remain pending in the present application, claims 10-24 having been cancelled previously *without prejudice* pursuant to the Examiner's restriction requirement and Applicant's decision to elect with traverse to prosecute the invention of original claims 1-9. Claims 1-5 and 26 have been cancelled *without prejudice* in order to seek expedited allowance of the instant application. Upon the indication of allowable subject matter, and before the issuance of any patent from this application, Applicant will give consideration to filing a divisional application for the claimed subject matter previously cancelled.

The amendment to the claims have been made to indicate that the present methods are directed to the use of noribogaine as a non-addictive analgesic agent to treat nociceptive pain in the absence of the treatment of drug dependency or drug abuse wherein the noribogaine is the sole analgesic agent which is administered. Thus, the present invention in claims 25 and 27-30 is essentially directed to the use of noribogaine as a substitute for morphine (or other opioid agonist) as the sole analgesic agent in the treatment of nociceptive pain as claimed. Claims 6-9 are directed to the use of noribogaine in combination with at least one opioid *antagonist* in the treatment of nociceptive pain under the same conditions as claim 25. Support for the amendment to the claims can be found throughout the originally filed application and claims and in particular, at page 3, first, second and third paragraphs, in particular in the second full paragraph, on page 4, in the first full paragraph, page 6, in the first paragraph, page 7, in the first full paragraph and the first few lines of the third full paragraph, on page 8 in the first full paragraph and in the examples. No new matter has been added by way of the present amendment.

The present application is directed to the unexpected discovery that noribogaine is a full opioid receptor agonist which acts as an antinociceptive agent, exhibiting antinociceptive activity similar to morphine's activity, without morphine's addiction to the patient. The present invention is directed to the use of noribogaine as an antinociceptive agent, similar to the effects obtained with morphine, but without the liability of abuse which occurs with typical opioid agonists such as morphine. Thus, the present invention represents a clear advance in the art and is deserving of patent protection.

The Examiner, having considered the previously filed amendment/response, has

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withdrawn all rejections from the previous office action. In the office action dated June 27, 2006, the Examiner has newly objected to or rejected the previously submitted claims variously under 35 U.S.C. §112, 103 and the cited prior art. For the reasons which are presented hereinbelow, it is respectfully submitted that the instantly amended claims are non-obvious over the cited prior art.

The Objection to Claims 27 and 28

The Examiner objects to previously filed claims 27 and 28 as containing a typo-type error. In order to obviate the Examiner's objection, claims 27 and 28 have been amended to refer to claims 25 and 26 respectively.

The Rejection of the Claims Under 35 U.S.C., First Paragraph

The Examiner has rejected the previously filed claims 6-9 and 25-30 for the reasons which are set forth in the office action on page 4. Essentially, it is the Examiner's position that the previously filed claims contained language which was not supported by the application. Applicant respectfully disagrees, inasmuch as the language in the application at page 8, first full paragraph clearly supports language in the previously filed claims. It is respectfully submitted that the term "in the absence of withdrawal symptoms associated with drug dependency" is fully supported by the language cited by the Examiner on page 5 of the office action, inasmuch as that language refers to the treatment options *in the alternative* which clearly provides treatment of one in the absence of the other. That is why the phrase contains the term "or" instead of the term "and".

However, notwithstanding Applicant's position and the clear support for the language in the previously filed claims, and in light of the Examiner's having provided alternative language that she finds acceptable, Applicants have amended the claims to reflect the Examiner's suggested language in order to obviate and remove this issue from the prosecution. Thus, the Examiner's rejection has been rendered moot.

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The Rejection of the Previously Filed Claims under 35 U.S.C. §103

The Examiner has rejected the previously filed claims as being unpatentable under 35 U.S.C. §103. It is the Examiner's contention that the previously presented claims are obvious over newly cited art for the reasons which appear in the office action. For the reasons which are clearly set forth in the sections which follow, Applicants respectfully submit that the instant claims are patentable over the cited references. It is noted here that the claimed invention sets forth that noribogaine is used in the treatment of nociceptive pain as the sole analgesic agent administered to the patient. The claims clearly disclaim and never intended to claim an invention in which an analgesic agent such as morphine or other addictive opiate analgesic was to be coadministered with noribogaine in the treatment of pain. The claims are clearly patentable over the cited art.

The Rejection of Previously Filed Claims 25 and 27-30 As Being Obvious Over Bagal, et al.

The Examiner contends that previously filed claims 25 and 27-30 are unpatentable as being obvious over the article "Modulation of Morphine-Induced Antinociception by Ibogaine and Noribogaine" by Bagal, et al., 1996, *Brain Research* 741, pages 258-262 (Bagal, et al.). It is the Examiner's view that Bagal, et al. teaches the use of noribogaine in combination with morphine for the treatment of pain and the previously filed claims read on such a method.

Although Applicant may take issue with some of the characterization of the teachings of Bagal, et al., as well as the significance and meaning of some of the claim language (e.g., consisting essentially of) which conflicts with prevailing caselaw and its relationship to the teachings of Bagal, et al., it is quite apparent that the instant claims clearly distinguish over any possible confusion which might exist that the claims read on a treatment of nociceptive pain using morphine in combination with noribogaine. In Bagal, et al., there is no teaching or suggestion, and the Examiner has not asserted a teaching or suggestion, that noribogaine could be used *itself* as a nociceptive agent in the absence of morphine. Consequently, the claimed invention is clearly patentable over Bagal, et al.

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The Rejection of Previously Filed Claims 6-9 As Being Obvious Over Bagal, et al. In View of Crain

The Examiner has rejected previously filed claims 6-9 as being obvious over Bagal, et al., in view of U.S. patent no. 5,580,876 (Crain) for the reasons which are stated in the office action on pages 7-9. In sum and substance, it is the Examiner's view that a combination of Bagal, et al. and Crain teachings that one could combine morphine and noribogaine as taught by Bagal, et al., with an opioid antagonist, as taught by Crain to obtain the invention of previously filed claims 6-9. Applicant traverses this rejection.

In order to address this rejection and obviate same, in light of the amendment to claims 25 and 27-30 which has been made herein from the suggestion of the Examiner on page 15 of the June 29, 2006 office action, Applicants have amended claims 6-9 to make it clear that the treatment of nociceptive pain using noribogaine and an opioid antagonist occurs in the absence of another analgesic agent such as morphine. It is clear from a reading of the prior art references, and the Examiner does not contend otherwise, that the cited prior art fails to disclose or teach the use of noribogaine in combination with an opioid antagonist in the absence of morphine because noribogaine was not recognized in the art *itself* as an antinociceptive agent. Because the art is clearly deficient in failing to recognize that noribogaine could be used to treat nociceptive pain without being combined with morphine, the present claims are patentable over the cited art.

The Rejection of Previously Filed Claims 25-30 as Being Unpatentable Over Pablo, et al.

The Examiner has rejected previously filed claims 25-30 as being unpatentable over the teachings of the article entitled "Noribogaine Stimulates Naloxone-Sensitive [35S]GTP γ S Binding" by Pablo, et al., *NeuroReport*, 9, pages 109-114, 1998 ("Pablo, et al."), in view of the article " κ -Opioid Receptors and Analgesia" by Mark J. Millan, *Trends in Pharmacological Sciences*, 1990, vol 11, pages 70-76 ("Millan") for the reasons which are set forth in the office action on pages 9-12 of the June 27, 2006 office action. Applicant respectfully traverses the Examiner's rejection and in order to obviate this rejection and advance prosecution of the present application, Applicant encloses her declaration which clearly shows that Pablo, et al. is not prior art to the instant application because Applicant is a co-author of that paper and was solely responsible for any invention disclosed in Pablo, et al. John P. Pablo, co-author of Pablo, et al., was a graduate student working in Applicant's research laboratory under her guidance and

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supervision, and did not contribute to any invention which was disclosed in Pablo, et al. Consequently, because Pablo, et al. is not prior art¹ to the present invention, the rejection of claims 25-30 based, in part, on Pablo, et al. is rendered moot.

Given that Pablo, et al. is not prior art to the instant invention, the Examiner's rejection of claims 25-30 based upon, in part, Pablo, et al., has been rendered moot.

The Rejection of Claims 6-9 as Being Unpatentable Over Pablo, et al. in view of Millan and further in view of Crain

The Examiner has rejected previously filed claims 6-9 as being unpatentable over Pablo, et al., in view of Millan and further in view of Crain for the reasons which are stated in the June 27, 2006 office action on pages 12-15. Applicants respectfully traverse the Examiner's rejection.

The enclosed Mash declaration is referenced here. It is clear from Applicant's declaration that Pablo, et al. is not prior art to the present application.² Millan and Crain, taken together, do not even mention noribogaine. It is clear from the disclosures that the claimed invention is patentable over the cited prior art.

The invention is clearly non-obvious over all of the cited prior art and is patentable.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and

1 Applicant also contends that Pablo, et al. is not prior art because Pablo, et al. was published *after* the filing of the priority provisional application s.n. 60/057,921, filed September 4, 1997. A reading of the priority application evidences support for the instant invention. Notwithstanding that support, Applicant provides the enclosed declaration to obviate this issue (See M.P.E.P. §715.01(c) and to expedite the allowance of the instant application. Applicant has not seen the need to argue that the instant application is nonetheless patentable over Pablo, et al and Millan for reasons related to deficiencies (in relationship to the present invention) in those references.

2 Applicants, through assertion of the enclosed Mash declaration, show that Pablo, et al. is not prior art, thus rendering the Examiner's rejection moot. Notwithstanding the fact that Pablo, et al. is not prior art, Applicants maintain their assertion that the instant invention is patentable over the combined prior art cited and present the Mash declaration here in an effort simply to expedite allowance of the instant application, without further presentation or polemic.

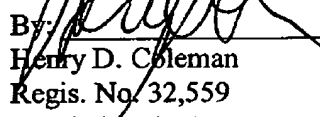
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such action is earnestly solicited.

Applicants have not added any claim and have canceled one dependent claim (claim 26). No fee is due for the presentation of this amendment. A notice of appeal is enclosed, as is a petition for an extension of time and a request to charge Deposit Account No. 04-0838. If any additional fee is due or any overpayment has been made, please charge/credit Deposit Account No. 04-0838. Should the Examiner wish to discuss the present application in an effort to advance its prosecution, the undersigned attorney may be reached at the telephone number set forth hereinbelow.

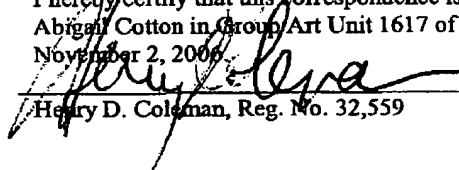
Respectfully submitted,
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Enclosure:
Mash Declaration
11/2/06

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I hereby certify that this correspondence is being sent by facsimile transmission to Examiner
Abigail Cotton in Group Art Unit 1617 of the United States Patent and Trademark office on
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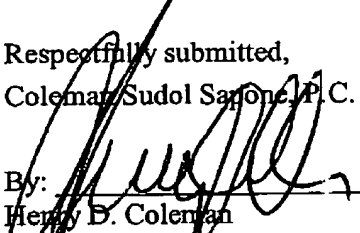
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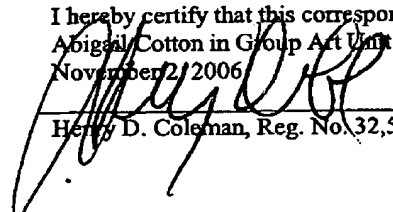
Respectfully submitted,
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